

REMARKS

Cancelled Claims

Applicant respectfully requests the indicated claims be cancelled. To the best of the undersigned's knowledge, Applicant does not cancel these claims for any reason related to patentability.

Double Patenting

Applicant respectfully requests the provisional double-patenting rejection be held in abeyance until the immediate claims are found allowable and a Terminal Disclaimer is required.

Obviousness Over VILLA combined with PETERSEN

The claims stand rejected as obvious over Marco VILLA *et al.*, *Method For the Preparation of Pure Citalopram*, U.S. Letters Patent No. 6,455,710 B1 (24 Sept. 2002), combined with Hans PETERSEN *et al.*, *Crystalline Base of Citalopram*, PCT Patent Application No. WO 01/68627 A1 (20 September 2001). The OFFICE ACTION, however, at page 5 invites Applicant to “demonstrate the criticality of the invention in view of the prior art.” I here respectfully provide this demonstration.

The art of record teaches the existence of the drug Citalopram. *See e.g.*, PETERSEN at page 1, lines 3-5; VILLA at col. 1, lines 7-9.

The art of record teaches away from the claimed invention

VILLA teaches that known Citalopram synthetic methods create unacceptable levels of an impurity called “desmethyl-citalopram.” *See* VILLA at col. 1, lines 50-57 (“The process ... has been found to give the desmethyl-citalopram derivative in unacceptable amounts.”). VILLA

thus teaches a way to eliminate desmethyl citalopram by using a cyanide exchange process. *See id.* at col. 3, lines 46 *et seq.*

The Inventors have found, however, that VILLA’s cyanide exchange process itself produces another impurity, 5-carboxamide –1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-phthalide, a carboxamide derivative illustrated in the application at “Formula 4.” *See* Specification at page 4, lines 1 *et seq.*

Neither VILLA nor PETERSEN mentions this contaminant. Neither VILLA nor PETERSEN appears to even recognize the existence of this contaminant, much less teach a way to eliminate it. To the contrary, VILLA teaches a cyanide exchange reaction which *creates* this contaminant. *See* Specification at page 4, lines 1 *et seq.*

The art of record fails to teach each claim element

The claimed invention provides a way to eliminate this contaminant. The claimed invention differs from the art of record by including several elements not found in the art of record, to produce a result not achieved by the art of record.

The claims require “presence of an iodide.” *See* claim 1, element (a). In contrast, neither VILLA nor PETERSEN mentions adding iodide to the reaction mixture. Furthermore, one of skill in the art would not read these references to suggest adding iodide.

The claims require use of “phosphorous oxyhalide” or “phosphorous oxide.” *See* claim 1, element (b). In contrast, VILLA does not mention phosphorous oxyhalide nor phosphorous oxide. To the contrary, the reference mentions no use of phosphorous at all.

A *prima facie* case of obviousness requires the art of record teach each element of the claims. *E.g.*, *In re Royka*, 409 F.2d 981 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385 (C.C.P.A. 1970). In the immediate case, the OFFICE ACTION fails to allege how the art of record teaches the claim limitations “presence of an iodide,” “phosphorous oxyhalide” and “phosphorous oxide.” The OFFICE ACTION thus fails to state a *prima facie* case.

The Inventors enjoy unexpected success

The treatment of citalopram with phosphorous oxychloride (POCl_3) removes two impurities, namely the carboxamide impurity and the desmethyl impurity. The claimed process converts the carboxamide impurity into the desired end-product. This is a significant advantage over the VILLA process, because the claimed invention increases both purity and yield.

The claimed invention works better than when the cyanide exchange reaction is carried out as per the teachings of VILLA in absence of added iodide. The Inventors provide evidence of this in the Specification. Tables II and III show that citalopram of about 70-78% purity is obtainable when the reaction is carried out in absence of added iodide, as per VILLA. In contrast, Examples 1 to 5 demonstrate preparation of citalopram of improved purity when the cyanide exchange reaction is carried out in presence of an iodide. Pointedly, the Specification examples provide data showing preparation of citalopram of purity > 94%.

These results would not have been expected by one of skill in the art. One of skill in the art would not read VILLA nor PETERSEN to suggest this result. There is a nexus between this evidence and the pending patent claims, because this evidence would be considered by one of

skill in the art to have probative value in showing the pending patent claims are non-obvious in light of the art of record.

Unexpected success is a secondary indicator of non-obviousness.

The art of record fails to suggest the combination

A *prima facie* case of obviousness requires the suggestion to combine the references be found somewhere in the art of record. *See In re Lee*, 277 F.3d 1338, 1340 (Fed. Cir. 2002). This means that somewhere in the art of record, some reference must suggest combining VILLA and PETERSEN. *See id.*

In the immediate case, the OFFICE ACTION fails to identify any teaching in the prior art of record which suggests the combination. Thus, the OFFICE ACTION fails to state a *prima facie* case.

PETERSEN Is not Available as a Reference

PETERSEN was published on 20 September 2001. In contrast, the immediate application claims priority from an India national patent application filed 7 January 2002, and an India national application filed 10 January 2002. *See* Form PTO-1390 (1 July 2004). (I attach copies of these two India national patent applications.) Thus, PETERSEN was published less than one year before the filing date of the immediate application. Thus, PETERSEN is not available as a reference.

An applicant may overcome a rejection based on a combination of references “by showing completion of the invention by applicant prior to the effective date of any of the references.” *See* M.P.E.P. § 715.02. In the immediate case, the priority India national

applications show completion of the invention prior to the effective date of PETERSEN. Thus, the rejection must be withdrawn.

Summary

Reconsideration is requested because prompt allowance of the claims is warranted.

Respectfully submitted,
PHARMACEUTICAL PATENT ATTORNEYS, LLC

_____/s/_____
By Mark POHL, Esq., USPTO Reg. No. 35,325

Enclosure : Rule 131 Declaration with *curriculum vitae*

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